



## SEQUENCE LISTING

<110> Wolfrain, Lawrence A  
Letterio, John J

<120> FUNCTIONALIZED TGF-BETA FUSION PROTEINS

<130> 4239-61302

<140> US 10/017,372

<141> 2001-10-19

<150> US 60/242,292

<151> 2000-10-20

<160> 39

<170> PatentIn version 3.1

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Asp Tyr Lys Asp Asp Asp Asp Lys  
1 5

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 1 5 10 15  
 tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc gga ctg tcc acc 96  
 Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
 20 25 30  
 tgc aag acc atc gac atg gag ctg gtg aag cgg aag cgc atc gag gcc 144  
 Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
 35 40 45  
 att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc ccc ccg agc 192  
 Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
 50 55 60  
 cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta ctg gct ctt 240  
 Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
 65 70 75 80  
 tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc gaa ccg gag 288  
 Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
 85 90 95  
 ccc gag cca gag gcg gac tac tac gcc aag gag gtc acc cgc gtg cta 336  
 Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
 100 105 110  
 atg gtg gaa agc ggc aac caa atc tat gat aaa ttc aag ggc acc ccc 384  
 Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
 115 120 125  
 cac agc tta tat atg ctg ttc aac acg tcg gag ctc cgg gaa gcg gtg 432  
 His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
 130 135 140  
 ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc ctg ctg agg ctc 480  
 Pro Glu Pro Val Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
 145 150 155 160  
 aag tta aaa gtg gag cag cac gtg gag cta tac cag aaa tac agc aat 528  
 Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
 165 170 175  
 gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc ccc agt gac tca 576

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser	
180 185 190	
ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg cgg cag tgg ctg	624
Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu	
195 200 205	
acc cgc aga gag gct ata gag ggt ttt cgc ctc agt gcc cac tct tcc	672
Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser	
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tct gac agc aaa gat aac aca ctc cac gtg gaa att aac ggg ttc aat	720
Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn	
225 230 235 240	
tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc atg aac cgg ccc	768
Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro	
245 250 255	
ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc cag cac ctg cac	816
Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His	
260 265 270	
agc tcc cgg cac cgc cga gac tac aag gat gac gac gac aag gcc ctg	864
Ser Ser Arg His Arg Arg Asp Tyr Lys Asp Asp Asp Asp Lys Ala Leu	
275 280 285	
gat acc aac tac tgc ttc agc tcc acg gag aag aac tgc tgc gtg cgg	912
Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg	
290 295 300	
cag ctc tac att gac ttc cgg aag gac ctg ggc tgg aag tgg att cat	960
Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His	
305 310 315 320	
gaa ccc aag ggc tac cat gcc aat ttc tgc ctg ggg ccc tgt ccc tac	1008
Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr	
325 330 335	
atc tgg agc cta gac act cag tac agc aag gtc ctg gct ctg tac aac	1056
Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn	
340 345 350	
cag cac aac ccg ggc gcg tgc gcg gcg ccg tgc tgc gtg ccg cag gcg	1104
Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala	
355 360 365	
ctg gag cca ctg ccc atc gtg tac tac gtg ggc cgc aag ccc aag gtg	1152
Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val	
370 375 380	
gag cag ctg tcc aac atg atc gtg cgt tcc tgc aag tgc agc tga	1197
Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser	
385 390 395	

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Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser  
210 215 220

Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Asp Tyr Lys Asp Asp Asp Asp Lys Ala Leu  
275 280 285

Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg  
290 295 300

Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His  
305 310 315 320

Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr  
325 330 335

Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn  
340 345 350

Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala  
355 360 365

Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val  
370 375 380

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 attcatgaac ccaagggcta ccatgccaat ttctgcctgg ggccctgtcc ctacatctgg 180  
 agcctagaca ctcagtacag caaggctcctg gctctgtaca accagcaciaa cccgggagcg 240  
 tcggcgagcg cgtgctgcgt gccgcaggcg ctggagccac tgcccatcgt gtactacgtg 300  
 ggccgcaagc ccaaggtgga gcagctgtcc aacatgatcg tgcgttcctg caagtgcagc 360  
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Ser Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe  
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Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His  
 35 40 45

Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr  
 50 55 60

Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala

65

70

75

80

Ser Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile  
                     85                    90                    95

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Ile Val Arg Ser Cys Lys Cys Ser  
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tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc gga ctg tcc acc 96  
 Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
                     20                    25                    30

tgc aag acc atc gac atg gag ctg gtg aag cgg aag cgc atc gag gcc 144  
 Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
                     35                    40                    45

att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc ccc ccg agc 192  
 Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
                     50                    55                    60

cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta ctg gct ctt 240  
 Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
 65                    70                    75                    80

tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc gaa ccg gag 288



Tyr	Asn	Ser	Thr	Arg	Asp	Arg	Val	Ala	Gly	Glu	Ser	Val	Glu	Pro	Glu			
				85					90					95				
ccc	gag	cca	gag	gcg	gac	tac	tac	gcc	aag	gag	gtc	acc	cgc	gtg	cta			336
Pro	Glu	Pro	Glu	Ala	Asp	Tyr	Tyr	Ala	Lys	Glu	Val	Thr	Arg	Val	Leu			
			100					105					110					
atg	gtg	gaa	agc	ggc	aac	caa	atc	tat	gat	aaa	ttc	aag	ggc	acc	ccc			384
Met	Val		Glu	Ser	Gly	Asn	Gln	Ile	Tyr	Asp	Lys	Phe	Lys	Gly	Thr	Pro		
			115					120					125					
cac	agc	tta	tat	atg	ctg	ttc	aac	acg	tcg	gag	ctc	cgg	gaa	gcg	gtg			432
His	Ser	Leu	Tyr	Met	Leu	Phe	Asn	Thr	Ser	Glu	Leu	Arg	Glu	Ala	Val			
			130				135					140						
ccg	gaa	cct	gta	ttg	ctc	tct	cgg	gca	gag	ctg	cgc	ctg	ctg	agg	ctc			480
Pro	Glu	Pro	Val	Leu	Leu	Ser	Arg	Ala	Glu	Leu	Arg	Leu	Leu	Arg	Leu			
					150					155					160			
aag	tta	aaa	gtg	gag	cag	cac	gtg	gag	cta	tac	cag	aaa	tac	agc	aat			528
Lys	Leu	Lys	Val	Glu	Gln	His	Val	Glu	Leu	Tyr	Gln	Lys	Tyr	Ser	Asn			
				165					170					175				
gat	tcc	tgg	cgc	tac	ctc	agc	aac	cgg	ctg	ctg	gcc	ccc	agt	gac	tca			576
Asp	Ser	Trp	Arg	Tyr	Leu	Ser	Asn	Arg	Leu	Leu	Ala	Pro	Ser	Asp	Ser			
				180				185					190					
ccg	gag	tgg	ctg	tcc	ttt	gat	gtc	acc	gga	ggt	gtg	cgg	cag	tgg	ctg			624
Pro	Glu	Trp	Leu	Ser	Phe	Asp	Val	Thr	Gly	Val	Val	Arg	Gln	Trp	Leu			
		195					200					205						
acc	cgc	aga	gag	gct	ata	gag	ggt	ttt	cgc	ctc	agt	gcc	cac	tct	tcc			672
Thr	Arg	Arg	Glu	Ala	Ile	Glu	Gly	Phe	Arg	Leu	Ser	Ala	His	Ser	Ser			
			210				215				220							
tct	gac	agc	aaa	gat	aac	aca	ctc	cac	gtg	gaa	att	aac	ggg	ttc	aat			720
Ser	Asp	Ser	Lys	Asp	Asn	Thr	Leu	His	Val	Glu	Ile	Asn	Gly	Phe	Asn			
					230					235					240			
tct	ggc	cgc	cgg	ggt	gac	ctg	gcc	acc	att	cac	ggc	atg	aac	cgg	ccc			768
Ser	Gly	Arg	Arg	Gly	Asp	Leu	Ala	Thr	Ile	His	Gly	Met	Asn	Arg	Pro			
				245					250				255					
ttc	ctg	ctc	ctc	atg	gcc	acc	ccg	ctg	gag	agg	gcc	cag	cac	ctg	cac			816
Phe	Leu	Leu	Leu	Met	Ala	Thr	Pro	Leu	Glu	Arg	Ala	Gln	His	Leu	His			
				260				265					270					
agc	tcc	cgg	cac	cgc	cga	gcc	ctg	gat	acc	aac	tac	tgc	ttc	agc	tcc			864
Ser	Ser	Arg	His	Arg	Arg	Ala	Leu	Asp	Thr	Asn	Tyr	Cys	Phe	Ser	Ser			
				275			280					285						
acg	gac	tac	aag	gat	gac	gac	gac	aag	gag	aag	aac	tgc	tgc	gtg	cgg			912
Thr	Asp	Tyr	Lys	Asp	Asp	Asp	Asp	Lys	Glu	Lys	Asn	Cys	Cys	Val	Arg			
				290			295				300							
cag	ctc	tac	att	gac	ttc	cgg	aag	gac	ctg	ggc	tgg	aag	tgg	att	cat			960
Gln	Leu	Tyr	Ile	Asp	Phe	Arg	Lys	Asp	Leu	Gly	Trp	Lys	Trp	Ile	His			

305	310	315	320	
gaa ccc aag ggc tac cat gcc aat ttc tgc ctg ggg ccc tgt ccc tac				1008
Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr	325	330	335	
atc tgg agc cta gac act cag tac agc aag gtc ctg gct ctg tac aac				1056
Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn	340	345	350	
cag cac aac ccg ggc gcg tgc gcg gcg ccg tgc tgc gtg ccg cag gcg				1104
Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala	355	360	365	
ctg gag cca ctg ccc atc gtg tac tac gtg ggc cgc aag ccc aag gtg				1152
Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val	370	375	380	
gag cag ctg tcc aac atg atc gtg cgt tcc tgc aag tgc agc tga				1197
Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser	385	390	395	

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			20					25					30		

Cys	Lys	Thr	Ile	Asp	Met	Glu	Leu	Val	Lys	Arg	Lys	Arg	Ile	Glu	Ala
		35					40					45			

Ile	Arg	Gly	Gln	Ile	Leu	Ser	Lys	Leu	Arg	Leu	Ala	Ser	Pro	Pro	Ser
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Gln	Gly	Asp	Val	Pro	Pro	Gly	Pro	Leu	Pro	Glu	Ala	Val	Leu	Ala	Leu
65					70					75				80	

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser  
210 215 220

Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser  
275 280 285

Thr Asp Tyr Lys Asp Asp Asp Asp Lys Glu Lys Asn Cys Cys Val Arg  
290 295 300

Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His  
 305 310 315 320

Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr  
 325 330 335

Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn  
 340 345 350

Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala  
 355 360 365

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 attcatgaac ccaagggtta ccatgccaat ttctgcctgg ggccctgtcc ctacatctgg 180  
 agcctagaca ctcagtacaa caaggctctg gctctgtaca accagcaciaa cccgggagcg 240  
 tcggcgggcg cgtgctgctg gccgcaggcg ctggagccac tgcccatcgt gtactacgtg 300  
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35 40 45

Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr  
50 55 60

Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala  
65 70 75 80

Ser Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile  
85 90 95

Val Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met  
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Ile Val Arg Ser Cys Lys Cys Ser  
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 <223> Encodes amino acid residues 1-5 of TGF-beta1

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 <222> (1197)..(1220)  
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 <223> Encodes ature fusion protein

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 agagcgctca tctcgatttt tacctgggtg gtatactgag acaccttggt gtcagagcct 180  
 caccgcgact cctgctgctt tctccctcaa cctcaaatta ttcaggacta tcacctacct 240  
 ttccttgga gacccaccc cacaagccct gcaggggcgg ggccctcgca tcccaccttt 300  
 gccgagggtt cccgctctcc gaagtgccgt ggggcgcgc ctcccc atg ccg ccc 356  
 Met Pro Pro  
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 tcg ggg ctg cgg cta ctg ccg ctt ctg ctc cca ctc ccg tgg ctt cta 404  
 Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Pro Trp Leu Leu  
 5 10 15  
 gtg ctg acg ccc ggg agg cca gcc gcg gga ctc tcc acc tgc aag acc 452  
 Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr Cys Lys Thr  
 20 25 30 35  
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 Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala Ile Arg Gly  
 40 45 50  
 cag atc ctg tcc aaa cta agg ctc gcc agt ccc cca agc cag ggg gag 548  
 Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser Gln Gly Glu  
 55 60 65

gta ccg ccc ggc ccg ctg ccc gag gcg gtg ctc gct ttg tac aac agc	596
Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu Tyr Asn Ser	
70 75 80	
acc cgc gac cgg gtg gca ggc gag agc gcc gac cca gag ccg gag ccc	644
Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu Pro Glu Pro	
85 90 95	
gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg cta atg gtg gac	692
Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp	
100 105 110 115	
cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata	740
Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile	
120 125 130	
tat atg ttc ttc aat acg tca gac att cgg gaa gca gtg ccc gaa ccc	788
Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro	
135 140 145	
cca ttg ctg tcc cgt gca gag ctg cgc ttg cag aga tta aaa tca agt	836
Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser	
150 155 160	
gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg	884
Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp	
165 170 175	
cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg	932
Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp	
180 185 190 195	
ctg tct ttt gac gtc act gga gtt gta cgg cag tgg ctg aac caa gga	980
Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu Asn Gln Gly	
200 205 210	
gac gga ata cag ggc ttt cga ttc agc gct cac tgc tct tgt gac agc	1028
Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Cys Ser Cys Asp Ser	
215 220 225	
aaa gat aac aaa ctc cac gtg gaa atc aac ggg atc agc ccc aaa cgt	1076
Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser Pro Lys Arg	
230 235 240	
cgg ggc gac ctg ggc acc atc cat gac atg aac cgg ccc ttc ctg ctc	1124
Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro Phe Leu Leu	
245 250 255	
ctc atg gcc acc ccc ctg gaa agg gcc cag cac ctg cac agc tca cgg	1172
Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His Ser Ser Arg	
260 265 270 275	
cac cgg aga gcc ctg gat acc aac gac tac aag gat gac gac gac aag	1220
His Arg Arg Ala Leu Asp Thr Asn Asp Tyr Lys Asp Asp Asp Asp Lys	
280 285 290	
gcc ctg gat acc aac tat tgc ttc agc tcc aca gag aag aac tgc tgt	1268

Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys	
295 300 305	
gtg cgg cag ctg tac att gac ttt agg aag gac ctg ggt tgg aag tgg	1316
Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp	
310 315 320	
atc cac gag ccc aag ggc tac cat gcc aac ttc tgt ctg gga ccc tgc	1364
Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys	
325 330 335	
ccc tat att tgg agc ctg gac aca cag tac agc aag gtc ctt gcc ctc	1412
Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu	
340 345 350 355	
tac aac caa cac aac ccg ggc gct tcg gcg tca ccg tgc tgc gtg ccg	1460
Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ser Pro Cys Cys Val Pro	
360 365 370	
cag gct ttg gag cca ctg ccc atc gtc tac tac gtg ggt cgc aag ccc	1508
Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro	
375 380 385	
aag gtg gag cag ttg tcc aac atg att gtg cgc tcc tgc aag tgc agc	1556
Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser	
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<220>  
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Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
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Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Asp Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser  
115 120 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val  
130 135 140

Pro Glu Pro Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu  
145 150 155 160

Lys Ser Ser Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asn Ser Trp Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Asn Gln Gly Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Cys Ser  
210 215 220

Cys Asp Ser Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser  
225 230 235 240

Pro Lys Arg Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Asp Tyr Lys Asp Asp  
275 280 285

Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys  
290 295 300

Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly  
305 310 315 320

Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu  
325 330 335

Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val  
340 345 350

Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ser Pro Cys  
355 360 365

Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly  
370 375 380

Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys  
385 390 395 400

Lys Cys Ser

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<211> 73

<212> DNA

<213> Artificial Sequence

<220>

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<400> 18

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ttcagctcca cgg 73

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caggtgctgg gc 72

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agagcgctca tctcgatttt taccctgggt gtatactgag acaccttggt gtcagagcct	180
caccgcgact cctgctgctt tctccctcaa cctcaaatta ttcaggacta tcacctacct	240
ttccttggga gacccacccc cacaagccct gcaggggcg ggcctccgca tcccaccttt	300
gccgaggggt cccgctctcc gaagtgccgt ggggcgccgc ctcccc atg ccg ccc	356
	Met Pro Pro
	1
tcg ggg ctg cgg cta ctg ccg ctt ctg ctc cca ctc ccg tgg ctt cta	404
Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Pro Trp Leu Leu	
5 10 15	
gtg ctg acg ccc ggg agg cca gcc gcg gga ctc tcc acc tgc aag acc	452
Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr Cys Lys Thr	
20 25 30 35	
atc gac atg gag ctg gtg aaa cgg aag cgc atc gaa gcc atc cgt ggc	500
Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala Ile Arg Gly	
40 45 50	
cag atc ctg tcc aaa cta agg ctc gcc agt ccc cca agc cag ggg gag	548
Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser Gln Gly Glu	
55 60 65	
gta ccg ccc ggc ccg ctg ccc gag gcg gtg ctc gct ttg tac aac agc	596
Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu Tyr Asn Ser	
70 75 80	
acc cgc gac cgg gtg gca ggc gag agc gcc gac cca gag ccg gag ccc	644
Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu Pro Glu Pro	
85 90 95	
gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg cta atg gtg gac	692
Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp	
100 105 110 115	
cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata	740
Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile	
120 125 130	
tat atg ttc ttc aat acg tca gac att cgg gaa gca gtg ccc gaa ccc	788
Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro	
135 140 145	
cca ttg ctg tcc cgt gca gag ctg cgc ttg cag aga tta aaa tca agt	836
Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser	
150 155 160	

gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg	884
Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp	
165 170 175	
cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg	932
Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp	
180 185 190 195	
ctg tct ttt gac gtc act gga gtt gta cgg cag tgg ctg aac caa gga	980
Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu Asn Gln Gly	
200 205 210	
gac gga ata cag ggc ttt cga ttc agc gct cac tgc tct tgt gac agc	1028
Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Cys Ser Cys Asp Ser	
215 220 225	
aaa gat aac aaa ctc cac gtg gaa atc aac ggg atc agc ccc aaa cgt	1076
Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser Pro Lys Arg	
230 235 240	
cgg ggc gac ctg ggc acc atc cat gac atg aac cgg ccc ttc ctg ctc	1124
Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro Phe Leu Leu	
245 250 255	
ctc atg gcc acc ccc ctg gaa agg gcc cag cac ctg cac agc tca cgg	1172
Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His Ser Ser Arg	
260 265 270 275	
cac cgg aga gcc ctg gat acc aac agc tac cca tac gac gtg cca gac	1220
His Arg Arg Ala Leu Asp Thr Asn Ser Tyr Pro Tyr Asp Val Pro Asp	
280 285 290	
tac gca tct ctg gcc ctg gat acc aac tat tgc ttc agc tcc aca gag	1268
Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu	
295 300 305	
aag aac tgc tgt gtg cgg cag ctg tac att gac ttt agg aag gac ctg	1316
Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu	
310 315 320	
ggt tgg aag tgg atc cac gag ccc aag ggc tac cat gcc aac ttc tgt	1364
Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys	
325 330 335	
ctg gga ccc tgc ccc tat att tgg agc ctg gac aca cag tac agc aag	1412
Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys	
340 345 350 355	
gtc ctt gcc ctc tac aac caa cac aac ccg ggc gct tcg gcg tca ccg	1460
Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ser Pro	
360 365 370	
tgc tgc gtg ccg cag gct ttg gag cca ctg ccc atc gtc tac tac gtg	1508
Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val	
375 380 385	

ggt cgc aag ccc aag gtg gag cag ttg tcc aac atg att gtg cgc tcc 1556  
 Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser  
           390                          395                          400

tgc aag tgc agc tga agccccgccc cgccccgccc ctcccggcag gcccgcccc 1611  
 Cys Lys Cys Ser  
           405

gcccccgccc cgc 1624

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 <223> Encodes amino acid residues 1-5 of TGF-beta1

<220>  
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 <223> Encodes HA epitope tag

<220>  
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 <222> (1182)..(1571)  
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Met Pro Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Pro  
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Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
           20                          25                          30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
           35                          40                          45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
           50                          55                          60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
 65                          70                          75                          80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
 100 105 110

Met Val Asp Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser  
 115 120 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val  
 130 135 140

Pro Glu Pro Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu  
 145 150 155 160

Lys Ser Ser Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
 165 170 175

Asn Ser Trp Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr  
 180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
 195 200 205

Asn Gln Gly Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Cys Ser  
 210 215 220

Cys Asp Ser Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser  
 225 230 235 240

Pro Lys Arg Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro  
 245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
 260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr Pro Tyr Asp  
 275 280 285

Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr Cys Phe Ser  
 290 295 300

Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg  
 305 310 315 320

Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala  
325 330 335

Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln  
340 345 350

Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser  
355 360 365

Ala Ser Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val  
370 375 380

Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile  
385 390 395 400

Val Arg Ser Cys Lys Cys Ser  
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accaactact gcttcagctc cacggagaag aactgctgcg tgcggcag 108

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ccgggagctg tgc 73

<210> 24  
<211> 1284  
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<213> Artificial Sequence

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<222> (1)..(1284)

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<223> Encodes mature fusion protein

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Met	His	Tyr	Cys	Val	Leu	Ser	Thr	Phe	Leu	Leu	Leu	His	Leu	Val	Pro	
1				5					10					15		

gtg	gcg	ctc	agt	ctg	tct	acc	tgc	agc	acc	ctc	gac	atg	gat	cag	ttt	96
Val	Ala	Leu	Ser	Leu	Ser	Thr	Cys	Ser	Thr	Leu	Asp	Met	Asp	Gln	Phe	
			20					25					30			

atg	cgc	aag	agg	atc	gag	gcc	atc	cgc	ggg	cag	atc	ctg	agc	aag	ctg	144
Met	Arg	Lys	Arg	Ile	Glu	Ala	Ile	Arg	Gly	Gln	Ile	Leu	Ser	Lys	Leu	
		35					40					45				

aag	ctc	acc	agc	ccc	ccg	gaa	gac	tat	ccg	gag	ccg	gat	gag	gtc	ccc	192
Lys	Leu	Thr	Ser	Pro	Pro	Glu	Asp	Tyr	Pro	Glu	Pro	Asp	Glu	Val	Pro	
	50					55					60					

ccg	gag	gtg	att	tcc	atc	tac	aac	agt	acc	agg	gac	tta	ctg	cag	gag	240
Pro	Glu	Val	Ile	Ser	Ile	Tyr	Asn	Ser	Thr	Arg	Asp	Leu	Leu	Gln	Glu	
65					70					75				80		

aag	gca	agc	cgg	agg	gca	gcc	gcc	tgc	gag	cgc	gag	cgg	agc	gag	cag	288
Lys	Ala	Ser	Arg	Arg	Ala	Ala	Ala	Cys	Glu	Arg	Glu	Arg	Ser	Glu	Gln	
				85					90					95		

gag	tac	tac	gcc	aag	gag	gtt	tat	aaa	atc	gac	atg	ccg	tcc	cac	ctc	336
Glu	Tyr	Tyr	Ala	Lys	Glu	Val	Tyr	Lys	Ile	Asp	Met	Pro	Ser	His	Leu	
			100					105							110	

ccc tcc gaa aat gcc atc ccg ccc act ttc tac aga ccc tac ttc aga Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg 115 120 125	384
atc gtc cgc ttt gat gtc tca aca atg gag aaa aat gct tcg aat ctg Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser Asn Leu 130 135 140	432
gtg aag gca gag ttc agg gtc ttc cgc ttg caa aac ccc aaa gcc aga Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg 145 150 155 160	480
gtg gcc gag cag cgg att gaa ctg tat cag atc ctt aaa tcc aaa gac Val Ala Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp 165 170 175	528
tta aca tct ccc acc cag cgc tac atc gat agc aag gtt gtg aaa acc Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr 180 185 190	576
aga gcg gag ggt gaa tgg ctc tcc ttc gac gtg aca gac gct gtg cag Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val Gln 195 200 205	624
gag tgg ctt cac cac aaa gac agg aac ctg ggg ttt aaa ata agt tta Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu 210 215 220	672
cac tgc ccc tgc tgt acc ttc gtg ccg tct aat aat tac atc atc ccg His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro 225 230 235 240	720
aat aaa agc gaa gag ctc gag gcg aga ttt gca ggt att gat ggc acc Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr 245 250 255	768
tct aca tat gcc agt ggt gat cag aaa act ata aag tcc act agg aaa Ser Thr Tyr Ala Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys 260 265 270	816
aaa acc agt ggg aag acc cca cat ctc ctg cta atg ttg ttg ccc tcc Lys Thr Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser 275 280 285	864
tac aga ctg gag tca caa cag tcc agc cgg cgg aag aag cgc gct ttg Tyr Arg Leu Glu Ser Gln Gln Ser Ser Arg Arg Lys Lys Arg Ala Leu 290 295 300	912
gat gct gcc gac tac aag gat gac gac gac aag gct ttg gat gct gcc Asp Ala Ala Asp Tyr Lys Asp Asp Asp Asp Lys Ala Leu Asp Ala Ala 305 310 315 320	960
tac tgc ttt aga aat gtg cag gat aat tgc tgc ctt cgc cct ctt tac Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg Pro Leu Tyr 325 330 335	1008

att gat ttt aag agg gat ctt gga tgg aaa tgg atc cat gaa ccc aaa 1056  
 Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys  
                   340                                  345                                  350

ggg tac aat gct aac ttc tgt gct ggg gca tgc cca tat cta tgg agt 1104  
 Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr Leu Trp Ser  
                   355                                  360                                  365

tca gac act caa cac acc aaa gtc ctc agc ctg tac aac acc ata aat 1152  
 Ser Asp Thr Gln His Thr Lys Val Leu Ser Leu Tyr Asn Thr Ile Asn  
                   370                                  375                                  380

ccc gaa gct tcc gct tcc cct tgc tgt gtg tcc cag gat ctg gaa cca 1200  
 Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp Leu Glu Pro  
                   385                                  390                                  395                                  400

ctg acc att ctc tat tac att gga aat acg ccc aag atc gaa cag ctt 1248  
 Leu Thr Ile Leu Tyr Tyr Ile Gly Asn Thr Pro Lys Ile Glu Gln Leu  
                                   405                                  410                                  415

tcc aat atg att gtc aag tct tgt aaa tgc agc taa 1284  
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<210> 25  
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<220>  
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 <222> (922)..(945)  
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                   20                                  25                                  30

Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu  
35 40 45

Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Asp Glu Val Pro  
50 55 60

Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu  
65 70 75 80

Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Glu Gln  
85 90 95

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Ser His Leu  
100 105 110

Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg  
115 120 125

Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser Asn Leu  
130 135 140

Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg  
145 150 155 160

Val Ala Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp  
165 170 175

Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr  
180 185 190

Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val Gln  
195 200 205

Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu  
210 215 220

His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro  
225 230 235 240

Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr  
245 250 255

Ser Thr Tyr Ala Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys  
260 265 270

Lys Thr Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser  
275 280 285

Tyr Arg Leu Glu Ser Gln Gln Ser Ser Arg Arg Lys Lys Arg Ala Leu  
290 295 300

Asp Ala Ala Asp Tyr Lys Asp Asp Asp Asp Lys Ala Leu Asp Ala Ala  
305 310 315 320

Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg Pro Leu Tyr  
325 330 335

Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys  
340 345 350

Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr Leu Trp Ser  
355 360 365

Ser Asp Thr Gln His Thr Lys Val Leu Ser Leu Tyr Asn Thr Ile Asn  
370 375 380

Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp Leu Glu Pro  
385 390 395 400

Leu Thr Ile Leu Tyr Tyr Ile Gly Asn Thr Pro Lys Ile Glu Gln Leu  
405 410 415

Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser  
420 425

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<211> 1303

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<222> (8)..(1303)

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	1					5					10					
gtc	ccg	gtg	gcg	ctc	agt	ctg	tct	acc	tgc	agc	acc	ctc	gac	atg	gat	97
Val	Pro	Val	Ala	Leu	Ser	Leu	Ser	Thr	Cys	Ser	Thr	Leu	Asp	Met	Asp	
15					20					25					30	
cag	ttt	atg	cgc	aag	agg	atc	gag	gcc	atc	cgc	ggg	cag	atc	ctg	agc	145
Gln	Phe	Met	Arg	Lys	Arg	Ile	Glu	Ala	Ile	Arg	Gly	Gln	Ile	Leu	Ser	
					35					40					45	
aag	ctg	aag	ctc	acc	agc	ccc	ccg	gaa	gac	tat	ccg	gag	ccg	gat	gag	193
Lys	Leu	Lys	Leu	Thr	Ser	Pro	Pro	Glu	Asp	Tyr	Pro	Glu	Pro	Asp	Glu	
					50					55					60	
gtc	ccc	ccg	gag	gtg	att	tcc	atc	tac	aac	agt	acc	agg	gac	tta	ctg	241
Val	Pro	Pro	Glu	Val	Ile	Ser	Ile	Tyr	Asn	Ser	Thr	Arg	Asp	Leu	Leu	
					65					70					75	
cag	gag	aag	gca	agc	cgg	agg	gca	gcc	gcc	tgc	gag	cgc	gag	cgg	agc	289
Gln	Glu	Lys	Ala	Ser	Arg	Arg	Ala	Ala	Ala	Cys	Glu	Arg	Glu	Arg	Ser	
					80					85					90	
gag	cag	gag	tac	tac	gcc	aag	gag	gtt	tat	aaa	atc	gac	atg	ccg	tcc	337
Glu	Gln	Glu	Tyr	Tyr	Ala	Lys	Glu	Val	Tyr	Lys	Ile	Asp	Met	Pro	Ser	
95					100					105					110	
cac	ctc	ccc	tcc	gaa	aat	gcc	atc	ccg	ccc	act	ttc	tac	aga	ccc	tac	385
His	Leu	Pro	Ser	Glu	Asn	Ala	Ile	Pro	Pro	Thr	Phe	Tyr	Arg	Pro	Tyr	
					115					120					125	

ttc aga atc gtc cgc ttt gat gtc tca aca atg gag aaa aat gct tcg Phe Arg Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser 130 135 140	433
aat ctg gtg aag gca gag ttc agg gtc ttc cgc ttg caa aac ccc aaa Asn Leu Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys 145 150 155	481
gcc aga gtg gcc gag cag cgg att gaa ctg tat cag atc ctt aaa tcc Ala Arg Val Ala Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser 160 165 170	529
aaa gac tta aca tct ccc acc cag cgc tac atc gat agc aag gtt gtg Lys Asp Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val 175 180 185 190	577
aaa acc aga gcg gag ggt gaa tgg ctc tcc ttc gac gtg aca gac gct Lys Thr Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala 195 200 205	625
gtg cag gag tgg ctt cac cac aaa gac agg aac ctg ggg ttt aaa ata Val Gln Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile 210 215 220	673
agt tta cac tgc ccc tgc tgt acc ttc gtg ccg tct aat aat tac atc Ser Leu His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile 225 230 235	721
atc ccg aat aaa agc gaa gag ctc gag gcg aga ttt gca ggt att gat Ile Pro Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp 240 245 250	769
ggc acc tct aca tat gcc agt ggt gat cag aaa act ata aag tcc act Gly Thr Ser Thr Tyr Ala Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr 255 260 265 270	817
agg aaa aaa acc agt ggg aag acc cca cat ctc ctg cta atg ttg ttg Arg Lys Lys Thr Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu 275 280 285	865
ccc tcc tac aga ctg gag tca caa cag tcc agc cgg cgg aag aag cgc Pro Ser Tyr Arg Leu Glu Ser Gln Gln Ser Ser Arg Arg Lys Lys Arg 290 295 300	913
gct ttg gat gct gcc agc tac cca tac gac gtg cca gac tac gca tct Ala Leu Asp Ala Ala Ser Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser 305 310 315	961
ctg gct ttg gat gct gcc tac tgc ttt aga aat gtg cag gat aat tgc Leu Ala Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys 320 325 330	1009
tgc ctt cgc cct ctt tac att gat ttt aag agg gat ctt gga tgg aaa Cys Leu Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys 335 340 345 350	1057

tgg atc cat gaa ccc aaa ggg tac aat gct aac ttc tgt gct ggg gca	1105
Trp Ile His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala	
355 360 365	
tgc cca tat cta tgg agt tca gac act caa cac acc aaa gtc ctc agc	1153
Cys Pro Tyr Leu Trp Ser Ser Asp Thr Gln His Thr Lys Val Leu Ser	
370 375 380	
ctg tac aac acc ata aat ccc gaa gct tcc gct tcc cct tgc tgt gtg	1201
Leu Tyr Asn Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val	
385 390 395	
tcc cag gat ctg gaa cca ctg acc att ctc tat tac att gga aat acg	1249
Ser Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Asn Thr	
400 405 410	
ccc aag atc gaa cag ctt tcc aat atg att gtc aag tct tgt aaa tgc	1297
Pro Lys Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys	
415 420 425 430	
agc taa	1303
Ser	

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<220>  
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Met His Tyr Cys Val Leu Ser Thr Phe Leu Leu Leu His Leu Val Pro
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Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe
20 25 30



Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu  
 35 40 45

Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Asp Glu Val Pro  
 50 55 60

Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu  
 65 70 75 80

Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Glu Gln  
 85 90 95

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Ser His Leu  
 100 105 110

Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg  
 115 120 125

Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser Asn Leu  
 130 135 140

Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg  
 145 150 155 160

Val Ala Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp  
 165 170 175

Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr  
 180 185 190

Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val Gln  
 195 200 205

Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu  
 210 215 220

His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro  
 225 230 235 240

Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr  
 245 250 255

Ser Thr Tyr Ala Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys  
260 265 270

Lys Thr Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser  
275 280 285

Tyr Arg Leu Glu Ser Gln Gln Ser Ser Arg Arg Lys Lys Arg Ala Leu  
290 295 300

Asp Ala Ala Ser Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala  
305 310 315 320

Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu  
325 330 335

Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile  
340 345 350

His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro  
355 360 365

Tyr Leu Trp Ser Ser Asp Thr Gln His Thr Lys Val Leu Ser Leu Tyr  
370 375 380

Asn Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln  
385 390 395 400

Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Asn Thr Pro Lys  
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Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser  
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<211> 1272

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<222> (1)..(1272)

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 1 5 10 15  
  
 aca atc agc ctc tct ctg tcc act tgc acc acg ttg gac ttc ggc cac 96  
 Thr Ile Ser Leu Ser Leu Ser Thr Cys Thr Thr Leu Asp Phe Gly His  
 20 25 30  
  
 atc aag aag aag agg gtg gaa gcc att agg gga cag atc ttg agc aag 144  
 Ile Lys Lys Lys Arg Val Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys  
 35 40 45  
  
 ctc agg ctc acc agc ccc cct gag cca tcg gtg atg acc cac gtc ccc 192  
 Leu Arg Leu Thr Ser Pro Pro Glu Pro Ser Val Met Thr His Val Pro  
 50 55 60  
  
 tat cag gtc ctg gca ctt tac aac agc acc cgg gag ttg ctg gaa gag 240  
 Tyr Gln Val Leu Ala Leu Tyr Asn Ser Thr Arg Glu Leu Leu Glu Glu  
 65 70 75 80  
  
 atg cac ggg gag agg gag gaa ggc tgc act cag gag acc tcg gag tct 288  
 Met His Gly Glu Arg Glu Glu Gly Cys Thr Gln Glu Thr Ser Glu Ser  
 85 90 95  
  
 gag tac tat gcc aaa gag atc cat aaa ttc gac atg atc cag gga ctg 336  
 Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu  
 100 105 110  
  
 gcg gag cac aat gaa ctg gcc gtc tgc ccc aaa gga att acc tct aag 384  
 Ala Glu His Asn Glu Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys  
 115 120 125  
  
 gtt ttt cgt ttc aat gtg tcc tca gtg gag aaa aat gga acc aat ctg 432  
 Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu  
 130 135 140  
  
 ttc cgg gca gag ttc cgg gtc ttg cgg gtg ccc aac ccc agc tcc aag 480

Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys	
145 150 155 160	
cgc aca gag cag aga att gag ctc ttc cag ata ctt cga ccg gat gag	528
Arg Thr Glu Gln Arg Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu	
165 170 175	
cac ata gcc aag cag cgc tac ata ggt ggc aag aat ctg ccc aca agg	576
His Ile Ala Lys Gln Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg	
180 185 190	
ggc acc gct gaa tgg ctg tct ttc gat gtc act gac act gtg cgc gag	624
Gly Thr Ala Glu Trp Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu	
195 200 205	
tgg ctg ttg agg aga gag tcc aac ttg ggt ctg gaa atc agc atc cac	672
Trp Leu Leu Arg Arg Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His	
210 215 220	
tgt cca tgt cac acc ttt cag ccc aat gga gac ata ctg gaa aat gtt	720
Cys Pro Cys His Thr Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Val	
225 230 235 240	
cat gag gtg atg gaa atc aaa ttc aaa gga gtg gac aat gaa gat gac	768
His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp	
245 250 255	
cat ggc cgt gga gac ctg ggg cgt ctc aag aag caa aag gat cac cac	816
His Gly Arg Gly Asp Leu Gly Arg Leu Lys Lys Gln Lys Asp His His	
260 265 270	
aac cca cac ctg atc ctc atg atg atc ccc cca cac cga ctg gac agc	864
Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser	
275 280 285	
cca ggc cag ggc agt cag agg aag aag agg gcc ctg gac acc aat gac	912
Pro Gly Gln Gly Ser Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Asp	
290 295 300	
tac aag gat gac gac gac aag gcc ctg gac acc aat tac tgc ttc cgc	960
Tyr Lys Asp Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Arg	
305 310 315 320	
aac ctg gag gag aac tgc tgt gta cgc ccc ctt tat att gac ttc cgg	1008
Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr Ile Asp Phe Arg	
325 330 335	
cag gat cta ggc tgg aaa tgg gtc cac gaa cct aag ggt tac tat gcc	1056
Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys Gly Tyr Tyr Ala	
340 345 350	
aac ttc tgc tca ggc cct tgc cca tac ctc cgc agc gca gac aca acc	1104
Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser Ala Asp Thr Thr	
355 360 365	
cat agc acg gtg ctt gga cta tac aac acc ctg aac cca gag gcg tct	1152
His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn Pro Glu Ala Ser	

370	375	380	
gcc tcg cca tgc tgc gtc ccc cag gac ctg gag ccc ctg acc atc ttg			1200
Ala Ser Pro Cys Cys Val Pro Gln Asp Leu Glu Pro Leu Thr Ile Leu			
385	390	395	400
tac tat gtg ggc aga acc ccc aag gtg gag cag ctg tcc aac atg gtg			1248
Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu Ser Asn Met Val			
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gtg aag tcg tgt aag tgc agc tga			1272
Val Lys Ser Cys Lys Cys Ser			
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Met	His	Leu	Gln	Arg	Ala	Leu	Val	Val	Leu	Ala	Leu	Leu	Asn	Leu	Ala
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Thr	Ile	Ser	Leu	Ser	Leu	Ser	Thr	Cys	Thr	Thr	Leu	Asp	Phe	Gly	His
		20						25					30		

Ile	Lys	Lys	Lys	Arg	Val	Glu	Ala	Ile	Arg	Gly	Gln	Ile	Leu	Ser	Lys
	35						40					45			

Leu	Arg	Leu	Thr	Ser	Pro	Pro	Glu	Pro	Ser	Val	Met	Thr	His	Val	Pro
	50					55					60				

Tyr	Gln	Val	Leu	Ala	Leu	Tyr	Asn	Ser	Thr	Arg	Glu	Leu	Leu	Glu	Glu
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

65

70

75

80

Met His Gly Glu Arg Glu Glu Gly Cys Thr Gln Glu Thr Ser Glu Ser  
85 90 95

Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu  
100 105 110

Ala Glu His Asn Glu Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys  
115 120 125

Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu  
130 135 140

Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys  
145 150 155 160

Arg Thr Glu Gln Arg Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu  
165 170 175

His Ile Ala Lys Gln Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg  
180 185 190

Gly Thr Ala Glu Trp Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu  
195 200 205

Trp Leu Leu Arg Arg Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His  
210 215 220

Cys Pro Cys His Thr Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Val  
225 230 235 240

His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp  
245 250 255

His Gly Arg Gly Asp Leu Gly Arg Leu Lys Lys Gln Lys Asp His His  
260 265 270

Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser  
275 280 285

Pro Gly Gln Gly Ser Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Asp  
290 295 300

Tyr Lys Asp Asp Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Arg  
 305 310 315 320

Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr Ile Asp Phe Arg  
 325 330 335

Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys Gly Tyr Tyr Ala  
 340 345 350

Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser Ala Asp Thr Thr  
 355 360 365

His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn Pro Glu Ala Ser  
 370 375 380

Ala Ser Pro Cys Cys Val Pro Gln Asp Leu Glu Pro Leu Thr Ile Leu  
 385 390 395 400

Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu Ser Asn Met Val  
 405 410 415

Val Lys Ser Cys Lys Cys Ser  
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Met His Leu Gln Arg Ala Leu Val Val Leu Ala Leu Leu Asn Leu Ala  
1 5 10 15

aca atc agc ctc tct ctg tcc act tgc acc acg ttg gac ttc ggc cac 96  
Thr Ile Ser Leu Ser Leu Ser Thr Cys Thr Thr Leu Asp Phe Gly His  
20 25 30

atc aag aag aag agg gtg gaa gcc att agg gga cag atc ttg agc aag 144  
Ile Lys Lys Lys Arg Val Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys  
35 40 45

ctc agg ctc acc agc ccc cct gag cca tcg gtg atg acc cac gtc ccc 192  
Leu Arg Leu Thr Ser Pro Pro Glu Pro Ser Val Met Thr His Val Pro  
50 55 60

tat cag gtc ctg gca ctt tac aac agc acc cgg gag ttg ctg gaa gag 240  
Tyr Gln Val Leu Ala Leu Tyr Asn Ser Thr Arg Glu Leu Leu Glu Glu  
65 70 75 80

atg cac ggg gag agg gag gaa ggc tgc act cag gag acc tcg gag tct 288  
Met His Gly Glu Arg Glu Glu Gly Cys Thr Gln Glu Thr Ser Glu Ser  
85 90 95

gag tac tat gcc aaa gag atc cat aaa ttc gac atg atc cag gga ctg 336  
Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu  
100 105 110

gcg gag cac aat gaa ctg gcc gtc tgc ccc aaa gga att acc tct aag 384  
Ala Glu His Asn Glu Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys  
115 120 125

gtt ttt cgt ttc aat gtg tcc tca gtg gag aaa aat gga acc aat ctg 432  
Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu  
130 135 140

ttc cgg gca gag ttc cgg gtc ttg cgg gtg ccc aac ccc agc tcc aag 480  
Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys  
145 150 155 160

cgc aca gag cag aga att gag ctc ttc cag ata ctt cga ccg gat gag 528  
Arg Thr Glu Gln Arg Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu  
165 170 175

cac ata gcc aag cag cgc tac ata ggt ggc aag aat ctg ccc aca agg 576  
His Ile Ala Lys Gln Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg  
180 185 190



ggc acc gct gaa tgg ctg tct ttc gat gtc act gac act gtg cgc gag Gly Thr Ala Glu Trp Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu 195 200 205	624
tgg ctg ttg agg aga gag tcc aac ttg ggt ctg gaa atc agc atc cac Trp Leu Leu Arg Arg Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His 210 215 220	672
tgt cca tgt cac acc ttt cag ccc aat gga gac ata ctg gaa aat gtt Cys Pro Cys His Thr Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Val 225 230 235 240	720
cat gag gtg atg gaa atc aaa ttc aaa gga gtg gac aat gaa gat gac His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp 245 250 255	768
cat ggc cgt gga gac ctg ggg cgt ctc aag aag caa aag gat cac cac His Gly Arg Gly Asp Leu Gly Arg Leu Lys Lys Gln Lys Asp His His 260 265 270	816
aac cca cac ctg atc ctc atg atg atc ccc cca cac cga ctg gac agc Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser 275 280 285	864
cca ggc cag ggc agt cag agg aag aag agg gcc ctg gac acc aat agc Pro Gly Gln Gly Ser Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Ser 290 295 300	912
tac cca tac gac gtg cca gac tac gca tct ctg gcc ctg gac acc aat Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn 305 310 315 320	960
tac tgc ttc cgc aac ctg gag gag aac tgc tgt gta cgc ccc ctt tat Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr 325 330 335	1008
att gac ttc cgg cag gat cta ggc tgg aaa tgg gtc cac gaa cct aag Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys 340 345 350	1056
ggt tac tat gcc aac ttc tgc tca ggc cct tgc cca tac ctc cgc agc Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser 355 360 365	1104
gca gac aca acc cat agc acg gtg ctt gga cta tac aac acc ctg aac Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn 370 375 380	1152
cca gag gcg tct gcc tcg cca tgc tgc gtc ccc cag gac ctg gag ccc Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro Gln Asp Leu Glu Pro 385 390 395 400	1200
ctg acc atc ttg tac tat gtg ggc aga acc ccc aag gtg gag cag ctg Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu 405 410 415	1248

tcc aac atg gtg gtg aag tcg tgt aag tgc agc tga  
 Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser  
 420 425

1284

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Thr Ile Ser Leu Ser Leu Ser Thr Cys Thr Thr Leu Asp Phe Gly His  
 20 25 30

Ile Lys Lys Lys Arg Val Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys  
 35 40 45

Leu Arg Leu Thr Ser Pro Pro Glu Pro Ser Val Met Thr His Val Pro  
 50 55 60

Tyr Gln Val Leu Ala Leu Tyr Asn Ser Thr Arg Glu Leu Leu Glu Glu  
 65 70 75 80

Met His Gly Glu Arg Glu Glu Gly Cys Thr Gln Glu Thr Ser Glu Ser  
 85 90 95

Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu  
 100 105 110

Ala Glu His Asn Glu Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys  
115 120 125

Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu  
130 135 140

Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys  
145 150 155 160

Arg Thr Glu Gln Arg Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu  
165 170 175

His Ile Ala Lys Gln Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg  
180 185 190

Gly Thr Ala Glu Trp Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu  
195 200 205

Trp Leu Leu Arg Arg Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His  
210 215 220

Cys Pro Cys His Thr Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Val  
225 230 235 240

His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp  
245 250 255

His Gly Arg Gly Asp Leu Gly Arg Leu Lys Lys Gln Lys Asp His His  
260 265 270

Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser  
275 280 285

Pro Gly Gln Gly Ser Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Ser  
290 295 300

Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn  
305 310 315 320

Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr  
325 330 335

Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys  
340 345 350

Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser  
355 360 365

Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn  
370 375 380

Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro Gln Asp Leu Glu Pro  
385 390 395 400

Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu  
405 410 415

Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser  
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           1                  5                  10

ccg ctg ctg tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc gga 97  
 Pro Leu Leu Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly  
       15                  20                  25

ctg tcc acc tgc aag acc atc gac atg gag ctg gtg aag cgg aag cgc 145  
 Leu Ser Thr Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg  
       30                  35                  40                  45

atc gag gcc att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc 193  
 Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser  
           50                  55                  60

ccc ccg agc cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta 241  
 Pro Pro Ser Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val  
           65                  70                  75

ctg gct ctt tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc 289  
 Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val  
           80                  85                  90

gaa ccg gag ccc gag cca gag gcg gac tac tac gcc aag gag gtc acc 337  
 Glu Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr  
       95                  100                  105

cgc gtg cta atg gtg gaa agc ggc aac caa atc tat gat aaa ttc aag 385  
 Arg Val Leu Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys  
       110                  115                  120                  125

ggc acc ccc cac agc tta tat atg ctg ttc aac acg tcg gag ctc cgg 433  
 Gly Thr Pro His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg  
           130                  135                  140

gaa gcg gtg ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc ctg 481  
 Glu Ala Val Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu  
           145                  150                  155

ctg agg ctc aag tta aaa gtg gag cag cac gtg gag cta tac cag aaa 529  
 Leu Arg Leu Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys  
           160                  165                  170

tac agc aat gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc ccc 577

Tyr	Ser	Asn	Asp	Ser	Trp	Arg	Tyr	Leu	Ser	Asn	Arg	Leu	Leu	Ala	Pro		
175						180					185						
agt	gac	tca	ccg	gag	tgg	ctg	tcc	ttt	gat	gtc	acc	gga	gtt	gtg	cgg	625	
Ser	Asp	Ser	Pro	Glu	Trp	Leu	Ser	Phe	Asp	Val	Thr	Gly	Val	Val	Arg		
190					195				200						205		
cag	tgg	ctg	acc	cgc	aga	gag	gct	ata	gag	ggg	ttt	cgc	ctc	agt	gcc	673	
Gln	Trp	Leu	Thr	Arg	Arg	Glu	Ala	Ile	Glu	Gly	Phe	Arg	Leu	Ser	Ala		
				210					215						220		
cac	tct	tcc	tct	gac	agc	aaa	gat	aac	aca	ctc	cac	gtg	gaa	att	aac	721	
His	Ser	Ser	Ser	Asp	Ser	Lys	Asp	Asn	Thr	Leu	His	Val	Glu	Ile	Asn		
			225					230					235				
ggg	ttc	aat	tct	ggc	cgc	cgg	ggg	gac	ctg	gcc	acc	att	cac	ggc	atg	769	
Gly	Phe	Asn	Ser	Gly	Arg	Arg	Gly	Asp	Leu	Ala	Thr	Ile	His	Gly	Met		
	240						245					250					
aac	cgg	ccc	ttc	ctg	ctc	ctc	atg	gcc	acc	ccg	ctg	gag	agg	gcc	cag	817	
Asn	Arg	Pro	Phe	Leu	Leu	Leu	Met	Ala	Thr	Pro	Leu	Glu	Arg	Ala	Gln		
	255						260					265					
cac	ctg	cac	agc	tcc	cgg	cac	cgc	cga	gcc	ctg	gat	acc	aac	gac	tac	865	
His	Leu	His	Ser	Ser	Arg	His	Arg	Arg	Ala	Leu	Asp	Thr	Asn	Asp	Tyr		
270					275					280					285		
aag	gat	gac	gac	gac	aag	gcc	ctg	gat	acc	aac	tac	tgc	ttc	agc	tcc	913	
Lys	Asp	Asp	Asp	Asp	Lys	Ala	Leu	Asp	Thr	Asn	Tyr	Cys	Phe	Ser	Ser		
				290					295					300			
acg	gag	aag	aac	tgc	tgc	gtg	cgg	cag	ctc	tac	att	gac	ttc	cgg	aag	961	
Thr	Glu	Lys	Asn	Cys	Cys	Val	Arg	Gln	Leu	Tyr	Ile	Asp	Phe	Arg	Lys		
			305					310					315				
gac	ctg	ggc	tgg	aag	tgg	att	cat	gaa	ccc	aag	ggc	tac	cat	gcc	aat	1009	
Asp	Leu	Gly	Trp	Lys	Trp	Ile	His	Glu	Pro	Lys	Gly	Tyr	His	Ala	Asn		
	320						325					330					
ttc	tgc	ctg	ggg	ccc	tgt	ccc	tac	atc	tgg	agc	cta	gac	act	cag	tac	1057	
Phe	Cys	Leu	Gly	Pro	Cys	Pro	Tyr	Ile	Trp	Ser	Leu	Asp	Thr	Gln	Tyr		
	335						340					345					
agc	aag	gtc	ctg	gct	ctg	tac	aac	cag	cac	aac	ccg	ggc	gcg	tcg	gcg	1105	
Ser	Lys	Val	Leu	Ala	Leu	Tyr	Asn	Gln	His	Asn	Pro	Gly	Ala	Ser	Ala		
350					355					360					365		
gcg	ccg	tgc	tgc	gtg	ccg	cag	gcg	ctg	gag	cca	ctg	ccc	atc	gtg	tac	1153	
Ala	Pro	Cys	Cys	Val	Pro	Gln	Ala	Leu	Glu	Pro	Leu	Pro	Ile	Val	Tyr		
				370					375					380			
tac	gtg	ggc	cgc	aag	ccc	aag	gtg	gag	cag	ctg	tcc	aac	atg	atc	gtg	1201	
Tyr	Val	Gly	Arg	Lys	Pro	Lys	Val	Glu	Gln	Leu	Ser	Asn	Met	Ile	Val		
			385					390					395				
cgt	tcc	tgc	aag	tgc	agc	tga	ggccccgccc	cgccacagc	cccccccc							1252	
Arg	Ser	Cys	Lys	Cys	Ser												

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<220>  
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Met Ala Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Leu  
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Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
 20 25 30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
 35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
 50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu

100

105

110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
 115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
 130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
 145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
 165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
 180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
 195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser  
 210 215 220

Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
 225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
 245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
 260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Asp Tyr Lys Asp Asp  
 275 280 285

Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys  
 290 295 300

Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly  
 305 310 315 320

Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu  
 325 330 335



Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val  
340 345 350

Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys  
355 360 365

Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly  
370 375 380

Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys  
385 390 395 400

Lys Cys Ser

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<220>  
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<223> Encodes FLAG epitope tage

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<222> (849)..(1226)

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ctg ccg ctg ctg tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc	98
Leu Pro Leu Leu Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala	
15 20 25	
gga ctg tcc acc tgc aag acc atc gac atg gag ctg gtg aag cgg aag	146
Gly Leu Ser Thr Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys	
30 35 40	
cgc atc gag gcc att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc	194
Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala	
45 50 55 60	
agc ccc ccg agc cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca	242
Ser Pro Pro Ser Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala	
65 70 75	
gta ctg gct ctt tac aac agt acc cgc gac cgg gta gcc ggg gaa agt	290
Val Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser	
80 85 90	
gtc gaa ccg gag ccc gag cca gag gcg gac tac tac gcc aag gag gtc	338
Val Glu Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val	
95 100 105	
acc cgc gtg cta atg gtg gaa agc ggc aac caa atc tat gat aaa ttc	386
Thr Arg Val Leu Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe	
110 115 120	
aag ggc acc ccc cac agc tta tat atg ctg ttc aac acg tcg gag ctc	434
Lys Gly Thr Pro His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu	
125 130 135 140	
cgg gaa gcg gtg ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc	482
Arg Glu Ala Val Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg	
145 150 155	
ctg ctg agg ctc aag tta aaa gtg gag cag cac gtg gag cta tac cag	530
Leu Leu Arg Leu Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln	
160 165 170	
aaa tac agc aat gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc	578
Lys Tyr Ser Asn Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala	
175 180 185	

ccc agt gac tca ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg Pro Ser Asp Ser Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val 190 195 200	626
cgg cag tgg ctg acc cgc aga gag gct ata gag ggt ttt cgc ctc agt Arg Gln Trp Leu Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser 205 210 215 220	674
gcc cac tgt tcc tgt gac agc aaa gat aac aca ctc cac gtg gaa att Ala His Cys Ser Cys Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile 225 230 235	722
aac ggg ttc aat tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc Asn Gly Phe Asn Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly 240 245 250	770
atg aac cgg ccc ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc Met Asn Arg Pro Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala 255 260 265	818
cag cac ctg cac agc tcc cgg cac cgc cga gcc ctg gat acc aac gac Gln His Leu His Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Asp 270 275 280	866
tac aag gat gac gac gac aag gcc ctg gat acc aac tac tgc ttc agc Tyr Lys Asp Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Ser 285 290 295 300	914
tcc acg gag aag aac tgc tgc gtg cgg cag ctc tac att gac ttc cgg Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg 305 310 315	962
aag gac ctg ggc tgg aag tgg att cat gaa ccc aag ggc tac cat gcc Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala 320 325 330	1010
aat ttc tgc ctg ggg ccc tgt ccc tac atc tgg agc cta gac act cag Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln 335 340 345	1058
tac agc aag gtc ctg gct ctg tac aac cag cac aac ccg ggc gcg tcg Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser 350 355 360	1106
gcg gcg ccg tgc tgc gtg ccg cag gcg ctg gag cca ctg ccc atc gtg Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val 365 370 375 380	1154
tac tac gtg ggc cgc aag ccc aag gtg gag cag ctg tcc aac atg atc Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile 385 390 395	1202
gtg cgt tcc tgc aag tgc agc tga ggccccgccc cgccccacagc cccgcccacc Val Arg Ser Cys Lys Cys Ser 400	1256

cggcaggccc ggccccaccc ccgcccgcct caccggggct gtatttaagg acatcgtgcc 1316  
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<220>  
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Met Ala Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Leu  
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Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
20 25 30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Cys Ser  
210 215 220

Cys Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Asp Tyr Lys Asp Asp  
275 280 285

Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys  
290 295 300

Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly  
305 310 315 320

Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu  
325 330 335

Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val  
 340 345 350

Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys  
 355 360 365

Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly  
 370 375 380

Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys  
 385 390 395 400

Lys Cys Ser

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           1                  5                  10  
  
 ccg ctg ctg tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc gga 97  
 Pro Leu Leu Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly  
       15                  20                  25  
  
 ctg tcc acc tgc aag acc atc gac atg gag ctg gtg aag cgg aag cgc 145  
 Leu Ser Thr Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg  
 30                  35                  40                  45  
  
 atc gag gcc att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc 193  
 Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser  
           50                  55                  60  
  
 ccc ccg agc cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta 241  
 Pro Pro Ser Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val  
           65                  70                  75  
  
 ctg gct ctt tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc 289  
 Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val  
       80                  85                  90  
  
 gaa ccg gag ccc gag cca gag gcg gac tac tac gcc aag gag gtc acc 337  
 Glu Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr  
       95                  100                  105  
  
 cgc gtg cta atg gtg gaa agc ggc aac caa atc tat gat aaa ttc aag 385  
 Arg Val Leu Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys  
 110                  115                  120                  125  
  
 ggc acc ccc cac agc tta tat atg ctg ttc aac acg tcg gag ctc cgg 433  
 Gly Thr Pro His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg  
           130                  135                  140  
  
 gaa gcg gtg ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc ctg 481  
 Glu Ala Val Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu  
           145                  150                  155  
  
 ctg agg ctc aag tta aaa gtg gag cag cac gtg gag cta tac cag aaa 529  
 Leu Arg Leu Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys  
       160                  165                  170  
  
 tac agc aat gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc ccc 577  
 Tyr Ser Asn Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro  
       175                  180                  185  
  
 agt gac tca ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg cgg 625

Ser	Asp	Ser	Pro	Glu	Trp	Leu	Ser	Phe	Asp	Val	Thr	Gly	Val	Val	Arg	
190					195					200					205	
cag	tgg	ctg	acc	cgc	aga	gag	gct	ata	gag	ggg	ttt	cgc	ctc	agt	gcc	673
Gln	Trp	Leu	Thr	Arg	Arg	Glu	Ala	Ile	Glu	Gly	Phe	Arg	Leu	Ser	Ala	
				210					215					220		
cac	tct	tcc	tct	gac	agc	aaa	gat	aac	aca	ctc	cac	gtg	gaa	att	aac	721
His	Ser	Ser	Ser	Asp	Ser	Lys	Asp	Asn	Thr	Leu	His	Val	Glu	Ile	Asn	
			225					230					235			
ggg	ttc	aat	tct	ggc	cgc	cgg	ggg	gac	ctg	gcc	acc	att	cac	ggc	atg	769
Gly	Phe	Asn	Ser	Gly	Arg	Arg	Gly	Asp	Leu	Ala	Thr	Ile	His	Gly	Met	
		240					245					250				
aac	cgg	ccc	ttc	ctg	ctc	ctc	atg	gcc	acc	ccg	ctg	gag	agg	gcc	cag	817
Asn	Arg	Pro	Phe	Leu	Leu	Leu	Met	Ala	Thr	Pro	Leu	Glu	Arg	Ala	Gln	
	255						260				265					
cac	ctg	cac	agc	tcc	cgg	cac	cgc	cga	gcc	ctg	gat	acc	aac	agc	tac	865
His	Leu	His	Ser	Ser	Arg	His	Arg	Arg	Ala	Leu	Asp	Thr	Asn	Ser	Tyr	
	270				275					280					285	
cca	tac	gac	gtg	cca	gac	tac	gca	tct	ctg	gcc	ctg	gat	acc	aac	tac	913
Pro	Tyr	Asp	Val	Pro	Asp	Tyr	Ala	Ser	Leu	Ala	Leu	Asp	Thr	Asn	Tyr	
			290						295					300		
tgc	ttc	agc	tcc	acg	gag	aag	aac	tgc	tgc	gtg	cgg	cag	ctc	tac	att	961
Cys	Phe	Ser	Ser	Thr	Glu	Lys	Asn	Cys	Cys	Val	Arg	Gln	Leu	Tyr	Ile	
			305					310					315			
gac	ttc	cgg	aag	gac	ctg	ggc	tgg	aag	tgg	att	cat	gaa	ccc	aag	ggc	1009
Asp	Phe	Arg	Lys	Asp	Leu	Gly	Trp	Lys	Trp	Ile	His	Glu	Pro	Lys	Gly	
		320					325					330				
tac	cat	gcc	aat	ttc	tgc	ctg	ggg	ccc	tgt	ccc	tac	atc	tgg	agc	cta	1057
Tyr	His	Ala	Asn	Phe	Cys	Leu	Gly	Pro	Cys	Pro	Tyr	Ile	Trp	Ser	Leu	
	335					340				345						
gac	act	cag	tac	agc	aag	gtc	ctg	gct	ctg	tac	aac	cag	cac	aac	ccg	1105
Asp	Thr	Gln	Tyr	Ser	Lys	Val	Leu	Ala	Leu	Tyr	Asn	Gln	His	Asn	Pro	
	350				355					360					365	
ggc	gcg	tcg	gcg	gcg	ccg	tgc	tgc	gtg	ccg	cag	gcg	ctg	gag	cca	ctg	1153
Gly	Ala	Ser	Ala	Ala	Pro	Cys	Cys	Val	Pro	Gln	Ala	Leu	Glu	Pro	Leu	
				370					375					380		
ccc	atc	gtg	tac	tac	gtg	ggc	cgc	aag	ccc	aag	gtg	gag	cag	ctg	tcc	1201
Pro	Ile	Val	Tyr	Tyr	Val	Gly	Arg	Lys	Pro	Lys	Val	Glu	Gln	Leu	Ser	
			385					390					395			
aac	atg	atc	gtg	cgt	tcc	tgc	aag	tgc	agc	tga	ggccccgccc	cgccccacagc				1254
Asn	Met	Ile	Val	Arg	Ser	Cys	Lys	Cys	Ser							
	400						405									
ccccgccacc	cggcaggccc	ggccccaccc	ccgcccgcct	caccgggggt	gtattttaagg											1314



acatcgtgcc ccaagccac ttgggatcga ttaaagcggc cgcgact

1361

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Met Ala Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Leu  
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Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
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Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro

115	120	125
His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val 130 135 140		
Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu 145 150 155 160		
Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn 165 170 175		
Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser 180 185 190		
Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu 195 200 205		
Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser 210 215 220		
Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn 225 230 235 240		
Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro 245 250 255		
Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His 260 265 270		
Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr Pro Tyr Asp 275 280 285		
Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr Cys Phe Ser 290 295 300		
Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg 305 310 315 320		
Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala 325 330 335		
Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln 340 345 350		

Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser  
 355 360 365

Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val  
 370 375 380

Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile  
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Val Arg Ser Cys Lys Cys Ser  
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ccg ctg ctg tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc gga	97
Pro Leu Leu Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly	
15 20 25	
ctg tcc acc tgc aag acc atc gac atg gag ctg gtg aag cgg aag cgc	145
Leu Ser Thr Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg	
30 35 40 45	
atc gag gcc att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc	193
Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser	
50 55 60	
ccc ccg agc cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta	241
Pro Pro Ser Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val	
65 70 75	
ctg gct ctt tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc	289
Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val	
80 85 90	
gaa ccg gag ccc gag cca gag gcg gac tac tac gcc aag gag gtc acc	337
Glu Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr	
95 100 105	
cgc gtg cta atg gtg gaa agc ggc aac caa atc tat gat aaa ttc aag	385
Arg Val Leu Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys	
110 115 120 125	
ggc acc ccc cac agc tta tat atg ctg ttc aac acg tcg gag ctc cgg	433
Gly Thr Pro His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg	
130 135 140	
gaa gcg gtg ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc ctg	481
Glu Ala Val Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu	
145 150 155	
ctg agg ctc aag tta aaa gtg gag cag cac gtg gag cta tac cag aaa	529
Leu Arg Leu Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys	
160 165 170	
tac agc aat gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc ccc	577
Tyr Ser Asn Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro	
175 180 185	
agt gac tca ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg cgg	625
Ser Asp Ser Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg	
190 195 200 205	

cag tgg ctg acc cgc aga gag gct ata gag ggt ttt cgc ctc agt gcc Gln Trp Leu Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala 210 215 220	673
cac tgt tcc tgt gac agc aaa gat aac aca ctc cac gtg gaa att aac His Cys Ser Cys Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn 225 230 235	721
ggg ttc aat tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc atg Gly Phe Asn Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met 240 245 250	769
aac cgg ccc ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc cag Asn Arg Pro Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln 255 260 265	817
cac ctg cac agc tcc cgg cac cgc cga gcc ctg gat acc aac agc tac His Leu His Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr 270 275 280 285	865
cca tac gac gtg cca gac tac gca tct ctg gcc ctg gat acc aac tac Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr 290 295 300	913
tgc ttc agc tcc acg gag aag aac tgc tgc gtg cgg cag ctc tac att Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile 305 310 315	961
gac ttc cgg aag gac ctg ggc tgg aag tgg att cat gaa ccc aag ggc Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly 320 325 330	1009
tac cat gcc aat ttc tgc ctg ggg ccc tgt ccc tac atc tgg agc cta Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu 335 340 345	1057
gac act cag tac agc aag gtc ctg gct ctg tac aac cag cac aac ccg Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro 350 355 360 365	1105
ggc gcg tcg gcg gcg ccg tgc tgc gtg ccg cag gcg ctg gag cca ctg Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu 370 375 380	1153
ccc atc gtg tac tac gtg ggc cgc aag ccc aag gtg gag cag ctg tcc Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser 385 390 395	1201
aac atg atc gtg cgt tcc tgc aag tgc agc tga ggccccgccc cgccccacagc Asn Met Ile Val Arg Ser Cys Lys Cys Ser 400 405	1254
cccgcccacc cggcaggccc ggccccacccc ccgcccgcct caccgggggt gtattttaagg	1314
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Met Ala Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Leu  
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Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
20 25 30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Cys Ser  
210 215 220

Cys Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr Pro Tyr Asp  
275 280 285

Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr Cys Phe Ser  
290 295 300

Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg  
305 310 315 320

Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala  
325 330 335

Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln  
340 345 350

Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser  
355 360 365

Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val  
370 375 380

BII  
Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile  
385 390 395 400

Val Arg Ser Cys Lys Cys Ser  
405

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